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COMMENTARY

Can RDoC Help Find Order in Thought Disorder?

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Thought disorder is a pernicious and nonspecific aspect of numerous serious mental illnesses (SMIs) and related conditions. Despite decades of empirical research on thought disorder, our present understanding of it is poor, our clinical assessments focus on a limited set of extreme behaviors, and treatments are palliative at best. Applying a Research Domain Criteria (RDoC) framework to thought disorder research offers advantages to explicate its phenotype; isolate its mechanisms; and develop more effective assessments, treatments, and potential cures. In this commentary, we discuss ways in which thought disorder can be understood within the RDoC framework. We propose operationalizing thought disorder within the RDoC construct of language using *psycholinguistic sciences*, to help objectify and quantify language within individuals; *technologically sophisticated paradigms*, to allow naturalistic behavioral sampling techniques with unprecedented ecological validity; and *computational modeling*, to account for a network of interconnected and dynamic linguistic, cognitive, affective, and social functions. We also highlight challenges for understanding thought disorder within an RDoC framework. Thought disorder likely does not occur as an isomorphic dysfunction in a single RDoC construct, but rather, as multiple potential dysfunctions in a network of RDoC constructs. Moreover, thought disorder is dynamic over time and context within individuals. In sum, RDoC is a useful framework to integrate multidisciplinary research efforts aimed at operationalizing, understanding, and ameliorating thought disorder.

Key words: language/serious mental illness/schizophrenia/computational psychiatry/psycholinguistics/disorganization

Why Do We Need an RDoC-Like Approach to Understand Thought Disorder?

Thought disorder, conceptualized as a "disruption in the interconnectivity of meaning and ideas within an individual," is a pernicious aspect of serious mental illness (SMI). As reviewed in Hart and Lewine,[1–3] thought disorder is a diagnostic criteria for schizophrenia- and bipolar-spectrum disorders (eg, pressured speech).[4] It is also observed in depression-spectrum, neurodegenerative and personality disorders and occurs in individuals under the influence of illicit substances and extreme stress.[5–8] Within psychiatric diagnostic groups, thought disorder is heterogeneous in its presentation, potentially involving a myriad of ineffectual and inefficient communicative behaviors.[9–11] As with many psychiatric conditions that suffer from within- and between-group heterogeneity, the mechanisms and causes of thought disorder have been difficult to delineate. More importantly, treatments are palliative at best, and offer only modest improvements in many cases.[12,13] Furthermore, private-sector investment for psychosis treatment has been deprioritized in recent years.[14] The National Institute of Mental Health[15] and others[16] have argued that improving mechanistic understanding of heterogeneous psychiatric "syndromes" requires dismantling them into basic constructs that span a full range of human behavior (ie, from normal to abnormal) and understanding them across varying levels of complexity (ie, from genetic to phenomenological). In this commentary, we explore how the Research Domain Criteria (RDoC) framework might be applied to the study of thought disorder.

How Can RDoC be Applied to the Study of Thought Disorder?

A first step in answering this question involves identifying the RDoC constructs and systems most relevant to formal thought disorder. Historically speaking, formal thought disorder is defined in terms of the "form" of communication; namely, the "way ideas, sentences and words are put together."[17] From a psycholinguistic perspective however, defining thought disorder is complicated, as it potentially involves both structural (eg,

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phonemic, syntactical) and semantic (ie, meaning) aspects of thought; both of which are observed in patients with SMI.[18–20] The RDoC construct of "language,"[21] defined as a "system of shared symbolic representations of the world, the self, and abstract concepts that support thought and communication," seems to capture many of these components.[22] Importantly, this construct is inclusive of a broad range of communicative behaviors and is not limited to expressive verbal functions that have been the primary focus of empirical investigation thus far. While verbal expression is an important vector for understanding thought disorder and language more broadly, other forms of communicative behaviors can be considered, such as nonverbal speech (eg, body expression), sign language, written expression, and potentially even other types of symbolic expression (eg, music, fashion, and art).[23–25] Symbolic expression using "nonverbal" media involves many of the same neural substrates as verbal language (eg, music,[26] gestures,[27] and math[28]), a notion formalized in theories about the origins of thought disorder in schizophrenia.[29] Moreover, clinical measures of thought disorder are often associated with measures of bizarre behavior (ie, nonverbal expression),[30,31] and measures of cognitive disorganization have been associated with increased creativity within the general population.[32] In sum, the RDoC language construct can be helpful for understanding thought disorder as an extreme variant of a potentially broad range of linguistic functions, which may help provide insight into its maladaptive and adaptive nature.[33]

If indeed the RDoC language construct can help understand thought disorder, how should language be measured within an RDoC framework? Historically, thought disorder has been operationalized using ordinal-level clinician-based rating scales/systems[1,11,34,35] that demonstrate face validity and clinical utility. These scales/systems have provided important information about thought disorder, for example, that it is multifaceted and reflects a broad range of behaviors such as derailment, tangentiality, circumstantiality, illogicality, and incoherence.[1,6] Moreover, it has been suggested that thought disorder is heritable[36]; a potential biomarker of psychiatric pathology[37]; and is associated with aberrant semantic processing[38,39]; neurocognitive liabilities[39]; and abnormalities in prefrontal,[40] left-temporal,[41] and anterior cingulate[42] brain regions.[43] That being said, rating-based approaches to measuring thought disorder are limited due to their reliance on ordinal scaling of clinician impression, which contributes to far from optimal inter-rater reliability (ie, reliability coefficients often below 0.70).[44] Moreover, they are calibrated with reference to a clinical population, hence, they are not well suited for examining constructs conceptualized as occurring on a continuum across the whole human population. Alternate approaches, such as behavioral coding of communication failures using interval and ratio scaling, have been developed.[6] These approaches have provided evidence that subtle forms of disorder are heritable,[45] more temporally stable than clinical thought disorder ratings,[46] and associated with impairments in relatively specific cognitive functions.[47–49] Unfortunately, these approaches are laborious and suffer from less than optimal reliability as well.[49] Within an RDoC framework, existing thought disorder measures may be useful for tapping "self-report" systems, however, they are far from optimal for quantifying "specific dimensions of observable behavior" across a "full range of human behavior."[22]

An alternate approach for understanding language production involves defining abnormalities based on "agnostic" statistical analysis of language features.[38,50] This approach is typified by the introduction of the Type-Token Ratio nearly 60 years ago[51] which is a relatively simple metric of lexical diversity, as well as newer more complex computational linguistic and statistical-based semantic analysis methods such latent semantic analysis (LSA).[52] LSA, for example, is a statistical approach to measuring meaning based on semantic distance, by allowing similarities among the elements of a language (eg, words, sentences, or passages) to be computed based on word co-occurrence patterns in large corpora of naturally produced discourse. Unlike standard keyword-based methods, LSA employs statistical and machine learning approaches to detect subtle aspects of semantic content. Similarities between words or documents are usually measured by the cosine between their vector representations in a high dimensional 'semantic space'. LSA has a rich history and has been used to address a broad range of commercial, organizational, theoretic, and computing issues.[52] Notably its technology is at the core of very successful automated essay scoring applications for academic purposes,[53] for measuring team performance in industry,[54] and has been used to reduce consumer fraud and identify theft.[55] As a tool with which to measure thought disorder, LSA can be used as a theory-driven model to assess the "semantic typicality" of language, and hence, identify and quantify tangents, incoherence, and other semantic disturbances.[56] This technique has also provided insight into the genetics, neural, and functional correlates of statistically deviant language use in SMI populations.[57–59] As of the writing of this commentary, "linguistic corpus-based analysis of language output" is a paradigm included in the RDoC matrix.

Importantly, quantifying an individual's "symbolic representations" cannot be done in a vacuum, as linguistic output changes dramatically as a function of task, topic, extrinsic motivational factors, and a host of social and environmental contextual influences. For example, someone's speech while driving a car in rush hour traffic will likely be different when talking with their spouse during a romantic candlelit dinner or while playing video games alone. Hence, the procedure for procuring language samples (ie, the "paradigm") requires careful

consideration. Historically speaking, assessment of both thought disorder and language expression has involved language generation tasks—involving responses to either standardized ambiguous (eg, Rorschach)[60] or unambiguous (eg, verbal fluency tests) stimuli, or behavioral observations—involving clinical interviews. However, there is little reason to assume that linguistic behavior observed during these relatively artificial interactions and tasks resembles linguistic behavior expressed as an individual navigates their natural environment. The last decade has seen technological, methodological, and analytic advances to allow for procurement of naturalistic language samples. These new techniques provide improved ecological validity, increased quantity of observations, and unobtrusive sampling that extends well beyond the confines of the clinic/laboratory compared to traditional sampling procedures. For example, data mining of social media is commonplace in science,[61] and analysis has successfully been used to model and predict exacerbations of psychiatric states.[62] Furthermore, ambulatory recording technologies (ie, assessing language as it manifests in one's daily environment) have been successfully and ethically implemented.[63] It is also now possible to integrate streams from other objective data sources (eg, ambulatory EEG, skin conductance, ambient acoustic signal), thus offering a powerful tool for modeling how systems (eg, cognitive, social, affective) and contextual factors modulate in concert. After all, as has been observed in some studies, thought disorder may primarily arise in specific contexts, for example, under high negative emotional states[64,65] or when cognitive resources are strained in some way.[66] In sum, while "traditional" paradigms for measuring language will likely continue to be important for understanding thought disorder, emerging technologies offer the potential for complementing this effort.

Potential Challenges in Applying RDoC to Thought Disorder

The RDoC initiative is unprecedented in scope and magnitude in mental health research and can help explicate thought disorder by systematically coordinating psycholinguistic, computational, psychological, and neuroscience efforts to understand language. There are some challenges in this regard.[67–69] First involves the reality that the language construct is closely inter-related with other RDoC-related cognitive, affective, and social constructs.[70,71] The neuroscience of language is fairly well established,[72] with a number of neural regions and connections identified that are critical to specific language functions. However, it is also well documented that language abilities are dependent on a broad range of cognitive (eg, working memory, declarative memory, attention), social (eg, social communication, affiliation, attachment), and affective (eg, effort valuation, acute threat) systems. In fact, theories exist asserting that these "nonlanguage" constructs are central to understanding thought disorder.[73,74] There is both experimental and correlational data to suggest that negative emotion exacerbates communication failures in patients with schizophrenia (ie, "affective reactivity")[64,65] and separately, that thought disorder reflects failures in basic cognitive abilities (eg, attention, working memory, and sequencing abilities).[47,73] It is likely that cognitive, affective, and social systems interact to produce thought disorder, and importantly, in potentially different ways. That is, thought disorder may reflect an "equifinality" from a diverse set of mechanisms, some embedded within traditionally defined language systems and others involving relatively distal systems. Relatedly, some prominent theories regarding thought disturbance (ie, "spreading activation" and "semantic associative network" theories)[75,76] assert that thought disorder manifests as a confluence of abnormally activated semantic networks and underactive/ineffectual executive/behavioral inhibition systems. Importantly, the latter systems can presumably occur from a variety of affective or cognitive abnormalities/states. Hence, modeling interactions between broadly-defined language, cognitive, affective, and social systems will likely be important for understanding thought disorder, and will require coordination across multiple RDoC constructs.

Second, thought disorder is by no means a static phenomenon, as it waxes and wanes on a moment to moment basis within individuals (eg, not every semantic unit produced is a similar tangent from the previous one). Moreover, its presentation likely qualitatively changes within individuals over time; presenting, for example, as incoherence in one situation or moment and unusual vocal prosodic expression the next (eg, it is physically impossible to produce most types of thought disorder simultaneously). Unfortunately, studies of thought disorder rarely consider its potentially dynamic nature. Nonetheless, understanding how thought disorder is dynamic both within people (eg, across time) and across people may hold information for diagnosis and treatment. For example, thought disorder may progressively exacerbate throughout the day in people with dementia, reflecting a gradual worsening as cognitive, affective, and other resources wane (ie, "sundowning"). In contrast, individuals with depression may show a very different pattern of thought disorder, perhaps waxing and waning when negativistic beliefs or emotions are activated.[77] Pressured speech, which is present in both bipolar disorder and schizophrenia, may be contextually dependent, such that it exacerbates with threat-related arousal in some individuals (eg, as seen with suspiciousness)[78] and reward-related or approach-system arousal in others (eg, as seen in mania).[79] To develop models sensitive to these different presentations, language will need to be operationalized and measured such that the resolution of its "signal" is scalable over time (eg, seconds, hours, days) and so it can be evaluated in concert with other events.

There is nothing inherent in the RDoC principles, or in the matrix, that hinders studying the dynamic nature of any construct, and the study of neurodevelopmental changes is explicitly encouraged.[22] Nonetheless, it may be challenging for the RDoC matrix to accommodate a construct whose phenotype changes both within people, potentially over relatively brief temporal epochs, and between people.

Summary and Conclusions: Integrating Psycholinguistics, Technologically Advanced Paradigms, and Computational Sciences

Despite decades of research on thought disorder, our present understanding of its nature is poor, our clinical assessment focuses on a limited set of extreme behaviors, and our treatments are far from optimal. The RDoC framework provides an interface for systematically coordinating efforts and integrating findings from a broad set of scientific disciplines across geographically and methodologically diverse research groups. To help advance scientific discovery of thought disorder, we propose that it be operationalized within the RDoc language construct using *psycholinguistic sciences*, to help objectify and quantify symbolic representations within individuals; using *technologically advanced paradigms*, to allow naturalistic behavioral sampling techniques with unprecedented ecological validity; and using *computational modeling*, to account for a network of interconnected and dynamic linguistic, cognitive, affective, and social functions. This endeavor is undoubtedly arduous and may seem insurmountable given the complexity of language more generally. In closing, it is worth considering that attempts to understand thought disorder and language from a computational perspective are not new. Ralph Hoffman's visionary work in the 1980s demonstrated the usefulness of computer simulations to understand language in SMI.[19,80] RDoC is not intended to be an integrative model accounting for all human functions, and may ultimately prove insufficient for providing information about thought disorder to spur more effective treatments and cures. Nonetheless, we believe that, at the very least, understanding thought disorder from an RDoC perspective is an important step in this process.

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